Primary Diastolic Heart Failure

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Abstract and Introduction

Abstract

Diastolic heart failure is defined clinically when signs and symptoms of heart failure are present in the presence of preserved le systolic function (ejection fraction >45%). The incidence and prevalence of primary diastolic heart failure increases with age an high as 50% in the elderly. Age, female gender, hypertension, coronary artery disease, diabetes and increased body mass ind factors for diastolic heart failure. Hemodynamic consequences such as increased pulmonary venous pressure, post-capillary p hypertension, and secondary right heart failure as well as decreased cardiac output are similar to those of systolic left ventricul although the nature of primary left ventricular dysfunction is different. Diagnosis of primary diastolic heart failure depends on th preserved left ventricular ejection fraction. Assessment of diastolic dysfunction is preferable but not mandatory. It is to be note levels of B-type natriuretic peptide does not distinguish between diastolic and systolic heart failure. Echocardiographic studies recommended to exclude hypertrophic cardiomyopathy, infiltrative heart disease, primary valvular heart disease, and constricti Myocardial stress imaging is frequently required to exclude ischemic heart disease. The prognosis of diastolic heart failure is v related to age, severity of heart failure, and associated comorbid diseases such as coronary artery disease. The prognosis of s heart failure is similar to that of systolic heart failure. However, cautious use of diuretics and/or nitrates may cause hypotensior state. Heart rate control is essential to improving ventricular filling. Pharmacologic agents such as angiotensin receptor blocker converting enzyme inhibitors, and calcium channel blockers are used in selected patients to decrease left ventricular hypertrop decrease myocardial fibrosis, aldosterone antagonists have a potential therapeutic role. However, prospective controlled studie required to establish their efficacy in primary diastolic heart failure.

Introduction

It is well established that the syndrome of heart failure can occur in the presence of both preserved and depressed ventricular function.[1,2] Primary diastolic heart failure is diagnosed when left ventricular (LV) ejection fraction is normal or near normal an systolic heart failure is diagnosed when there is a decrease in LV ejection fraction. It should be appreciated, however, that abn diastolic or systolic function do not always cause clinical heart failure. Furthermore, in both primary systolic and diastolic heart indices of systolic and diastolic function may be abnormal. For example, in dilated cardiomyopathy with a marked increase in v diastolic pressure, a restrictive transmitral flow pattern (diastolic dysfunction) is frequently present. Similarly, in primary diastoli although the ejection fraction is normal, myocardial contractile function may be depressed. It is also recognized that the phase following completion of ejection until the closure of the semilunar valves (hang-out time) is related to myocardial relaxation. Th relaxation and rapid filling phases are also markedly influenced by systolic function.[3] Thus, systolic and diastolic phases and f interdependent.

The clinical manifestations and hemodynamic consequences of diastolic and systolic heart failure may be similar, although the pathophysiologic mechanisms are different. Decreased ventricular compliance (increased stiffness) and abnormal diastolic fillir principal functional abnormalities in patients with diastolic heart failure.[4,5] Decreased LV compliance is associated with a disp elevation of its diastolic pressure, which causes a passive increase in left atrial and pulmonary venous pressures, which produ of pulmonary venous congestion. Passive increase in pulmonary artery pressure (post-capillary pulmonary hypertension), whe mechanism of secondary right ventricular failure associated with increased right ventricular diastolic and right atrial pressure a symptoms of systemic venous hypertension. With a marked restriction in ventricular filling stroke volume may decline due to de preload associated with signs and symptoms of low cardiac output.

In primary systolic failure, a reduced LV ejection fraction is the initial functional derangement, which is associated with a dispro

increase in end-systolic and end-diastolic volumes and pressures and a passive increase in left atrial and pulmonary venous p hemodynamic mechanism of signs and symptoms of pulmonary venous congestion. Post-capillary pulmonary hypertension an failure is associated with signs and symptoms of systemic venous hypertension. A decrease in forward stroke volume and carc also occur due to reduced ejection fraction. The mechanism of hemodynamic consequences in primary diastolic heart failure is Table 1. It is apparent that it is difficult to distinguish between diastolic and systolic heart failure by clinical and hemodynamic p

Definition and Diagnosis of Primary Diastolic Heart Failure

As the principal functional derangement in diastolic heart failure is decreased compliance (increased stiffness),[5] which is assc upward shift of the LV diastolic pressure volume curve, a pathophysiologic definition has been proposed based on these functi abnormalities. The proposed pathophysiologic definition is "a condition resulting from an increased resistance to filling of one c ventricles, leading to symptoms of congestion due to an inappropriate upward shift of the diastolic pressure-volume relation (th terminal phase of the cardiac cycle)."[3] Although this definition describes the principal pathophysiologic mechanism of primary failure, it is not clinically applicable, as it is difficult to determine the pressure-volume curves in routine clinical practice. A more definition that can be easily applied in clinical practice is "a condition with classic findings of congestive failure, with abnormal c normal systolic function at rest." The proposed diagnostic criteria, which can be applied in most clinical circumstances, are 1) c evidence of congestive heart failure; 2) objective evidence of normal LV systolic function; and 3) objective evidence of LV diast (relaxation, filling, distensibility).[6,7]

Diagnosis of congestive heart failure can be made clinically in the vast majority of patients if the symptoms of pulmonary venou (paroxysmal nocturnal dyspnea, orthopnea) and/or systemic venous hypertension (dependent edema) are present, along with radiologic findings of increased LV diastolic pressure (S4, S3 gallops), pulmonary venous pressure (chest x-ray), pulmonary ar (increased pulmonic component of the second heart sound), and right ventricular failure (S3 gallop, elevated jugular venous pr hepatomegaly, peripheral edema). It should be appreciated that it is not necessary for all the symptoms and signs to be preser patients for the diagnosis of heart failure. Indeed, in some patients with suspected heart failure, many or all the physical findinç lacking. In occasional patients, cardiopulmonary exercise testing, pulmonary function tests, exercise echo-Doppler studies, anc of hemodynamics at rest and during exercise are necessary to distinguish between symptoms of cardiac and noncardiac origir

A few recent studies have also suggested that higher than normal plasma levels of atrial and brain natriuretic peptide indicate l Clinical diagnosis of heart failure is often based on physicians' subjective impressions. To overcome the subjectivity, various cı been proposed in various studies. The criteria used in the Framingham study, initially proposed for the diagnosis of congestive have been used for the diagnosis of diastolic heart failure in some studies (Table 2).[8] For establishing a definite diagnosis of (heart failure in this study, two major or one major and two minor criteria had to be present concurrently. When these diagnostic used, it is likely that more symptomatic patients with moderate and severe heart failure will be identified and patients with milde may be missed.

The objective evidence of normal LV systolic function is more frequently established in clinical practice by determining the ejec echocardiography or radionuclide ventriculography. At the bedside, although a normal LV apical impulse usually indicates a nc ejection fraction, a sustained LV impulse, which is most frequently associated with a reduced ejection fraction, may also be pre with marked LV hypertrophy with normal ejection fractions. Thus, for clinical purposes, echocardiographic or radionuclide ventı evaluation of LV systolic function should be considered in all patients with clinically confirmed or suspected heart failure.

During initial evaluation, echocardiography and Doppler studies are preferable, as additional information regarding valvular hez thickness, mass atrial enlargement, and LV diastolic, right ventricular systolic, and systemic venous pressures can be obtainec

There is controversy regarding the definition of preserved ejection fraction; in some studies, 50% or higher[9] and in others, 45' has been regarded as normal and has been used for the diagnosis of diastolic heart failure. In clinical practice, most frequently ejection fraction of 45%, estimated by echocardiography, is used to define preserved LV systolic function.

Assessment of the neurohormonal profile has been suggested to distinguish between preserved and depressed LV ejection fre Increased levels of N-terminal atrial natriuretic peptide (ANP) and brain natriuretic peptide (BNP) have been shown to indicate ejection fraction.[11] However, recent studies have also reported that in patients with clinical heart failure and a normal ejection endothelin-1, norepinephrine, ANP, and BNP levels are increased.[12] Furthermore, higher BNP levels have been reported to ir prognosis in patients with primary diastolic heart failure.[12] Thus, estimation of BNP may be useful for the diagnosis of clinical rather than for estimation of the ejection fraction.[13]

After establishing the presence of preserved LV systolic function, it is desirable to assess LV diastolic function; however, it is n document the type and/or severity of diastolic dysfunction in patients with overt clinical heart failure.[1,2] Various indices of dias relaxation, chamber and myocardial stiffness, diastolic pressure-volume curves, and diastolic filling characteristics -- can be as either invasive or noninvasive techniques.[14] In clinical practice, echo-Doppler studies are preferable and can provide informat relaxation (e.g., isovolumic relaxation time), abnormalities of filling (e.g., abnormal early filling/atrial filling velocity ratio), and ch

diastolic pressure (e.g., restrictive transmitral filling pattern, abnormal pulmonary venous flow patterns). During radionuclide ve study to measure the LV ejection fraction, it is also possible to assess diastolic function by determining the peak filling rate and filling.

It should be appreciated that clinical heart failure with preserved systolic function (diastolic heart failure) can be caused by hete pathophysiologic conditions. Hypertrophic cardiomyopathy, infiltrative cardiomyopathies such as amyloidosis, valvular heart dis constrictive pericarditis, endocardial fibroelastosis, and other forms of restrictive cardiomyopathy can cause similar clinical syn may need to be excluded by specific investigations before the diagnosis of "primary" diastolic heart failure is established. The that can be used in clinical practice are summarized in Table 3.

Prevalence of Primary Diastolic Heart Failure and Associated Pathophysiologic Disorders

The true incidence and prevalence of primary diastolic heart failure is difficult to estimate, as most studies are not prospective performed in referral institutions. In the Study of LV Dysfunction (SOLVD) registry, approximately 30% of patients with the diag failure had preserved LV systolic function.[15-19] In a number of retrospective studies, the reported incidence of diastolic heart f between 20%-40%.[15] The community studies reported an incidence as high as 50%.[18] In all studies, however, it has been o the incidence increases with age. In patients less than 60 years old, the incidence is about 15%-25%; between 60-70 years old 40%; and in patients 70 years old or older, approximately a 50% incidence of diastolic heart failure has been observed. The inc higher in elderly women. The reasons for a higher incidence in females than in males are not entirely clear. Why primary diastc more common in the elderly is also not clear. Age-related changes in the myocardial structure and function and changes in the neuroendocrine profile have been suggested as contributing factors.[20]

In animal studies, it has been observed that myocardial cell size increases with age. The collagen content of the myocardium a The sarcoplasmic reticular calcium ATPase activity (SERCA), which is necessary for appropriate calcium reuptake and initiatio relaxation, has been found to be decreased in senescent hearts. The overexpression of SERCA in senescent hearts in transge has been shown to enhance myocardial relaxation and contractile function. The neuroendocrine changes with aging, such as c adrenergic receptor density, decreased b-adrenergic inotropic response, and increased angiotensinogen and angiotensin-conv (ACE) concentrations and angiotensin receptors, may be contributing factors for myocyte hypertrophy and increased myocardi content.

Age-related changes in vascular and cardiac function might also be contributing factors in the higher incidence of diastolic hea elderly population. The compliance of the aorta and of large- and medium-size arteries is substantially decreased. The reflecte arterial pulsation may be accentuated and may occur during systole, which increases the resistance to LV ejection, and may c hypertrophy, which is associated with impaired diastolic function. Calculated LV mass is usually increased, but the contractile f ejection function remain unchanged. With aging, the early filling rate is decreased, which is compensated by increased late filli evident from the decreased E/A ratio in the transmitral flow pattern. In the elderly population, the incidence of systolic hyperten which may be associated with LV hypertrophy, an important contributing factor to diastolic heart failure. Furthermore, in the eld incidence of coronary artery disease (CAD) also increases, which may produce ischemia-induced LV diastolic dysfunction. The contributing factors in the genesis of diastolic heart failure are summarized in Table 4.

"Primary diastolic heart failure" appears to be a "clinical syndrome" of the elderly. The most frequent etiologic association, parti elderly population, is hypertension with or without CAD (Table 5).[21] However, the incidence of clinically silent, significant CAD considerable in diastolic heart failure.[22] Diabetes is also a relatively frequent pathophysiologic association. In African America obesity, and increased body mass index appear to be more important associations than in Caucasians (Table 6).[23] Thus, the clinical profile may aid in the diagnosis of primary diastolic heart failure. Furthermore, it is relevant to the therapeutic interventic prevention of this syndrome. It should be emphasized that irrespective of race and gender, hypertension is the most frequent e association of primary diastolic heart failure and adequate control of hypertension is necessary to decrease its incidence.

Prognosis of Primary Diastolic Heart Failure

Prospective and controlled studies to assess prognosis and the natural history are lacking, and a wide range of mortality and n been observed.[1,15] In some studies, a 5-year mortality of 50% was observed and was similar to that of primary systolic heart similar mortality rates in patients with diastolic and systolic heart failure in this study were independent of the incidence of hype CAD. In a community-based study, 1-, 2-,and 3-year mortality of 29%, 39%, and 60%, respectively, were reported.[24] In contra patients with new-onset heart failure in the outpatient setting, 2-year mortality of patients with preserved LV systolic function wa significantly less than the 2-year mortality of patients with systolic heart failure (19%).[25] The hospitalization rates were also lo with diastolic heart failure. The explanation for these wide differences in the observed incidences of mortality and morbidity in t not apparent. There are no obvious differences in race, gender, or age of the population studied, and the incidences of a histo hypertension, diabetes, or CAD were also similar. The severity of clinical heart failure of patients in these studies might have b which might explain, to some extent, the differences in the observed incidences of mortality and morbidity of primary diastolic h these studies.

The presence of CAD is associated with poor prognosis, particularly in the elderly. Aronow et al.[26] reported 1-, 2-, 3-, and 4-y rates of 22%, 38%, 46%, and 56%, respectively, in 166 patients with an average age of 82 years, all with CAD. In the absence CAD, the prognosis appears more favorable. Zile et al.[27] reported annual mortality of approximately 2% in patients without C/ hypertrophy. Brogan et al.[28] studied 53 patients without coronary artery and valvular heart disease, confirmed by cardiac cath history of hypertension was present in 83%, and diabetes in 30% of patients. In 15% of patients, LV hypertrophy was documer average follow-up of 68 months, there was only one cardiac death. Thus, it appears that in the absence of significant LV hyper myocardial ischemia (idiopathic primary diastolic heart failure), the overall prognosis may not be as unfavorable as has been o some studies. However, controlled, prospective studies will be necessary for appropriate assessment of the prognosis of patie diastolic heart failure. Age, clinical severity of heart failure, degree of LV hypertrophy, myocardial ischemia resulting from CAD, other comorbid conditions, such as renal failure, will remain important determinants of long-term prognosis of primary diastolic

Therapeutic Approaches

The objectives and the potential therapeutic approaches for primary diastolic heart failure are outlined in Table 7. Most patient symptoms related to pulmonary and systemic venous hypertension. Diuretics, nitrates, ACE inhibitors, and angiotensin II subty receptor blocking agents decrease right atrial and pulmonary capillary wedge pressures and are useful in relieving congestive Indeed, diuretic therapy is required in almost all symptomatic patients. However, diuretics and nitrates should be used cautious excessive diuretics and nitrates may decrease cardiac output and induce hypotension and renal failure. The doses of diuretics should be adjusted according to improvement in symptoms and changes in weight. Although ACE inhibitors and AT1 blockers pulmonary and systemic venous pressures, they may also induce hypotension and renal failure and therefore should be used

Several drugs have the potential to improve ventricular relaxation (lusitropic effect). The drugs that increase myocardial cyclic monophosphate concentrations, such as b-adrenergic agonists and cardiac-specific phosphodiesterase inhibitors, may also er myocardial relaxation.[29] Clinically available b adrenergic agonists and phosphodiesterase inhibitors can be administered only and therefore can be used for short-term treatment only. Furthermore, these agents can also induce malignant ventricular arrh the clinical usefulness of these drugs is limited.

Phospholamban inhibition and enhanced SERCA are associated with increased myocardial relaxation; however, drugs targete these objectives are not available. Nitric oxide promoters also have the potential to improve relaxation and diastolic function. T effect of nitrates may be partly mediated by nitric oxide.

Controversy exists about the potential role of digitalis therapy in patients with preserved systolic function in sinus rhythm. In the Investigation Group (DIG) trials,[30] 988 patients with congestive heart failure had LV ejection fractions greater than 45%. The i.e., the combined incidence of death and hospitalization for treatment of heart failure, were similar to those in patients with red ejection fractions.[15,30] However, digitalis therapy presently should be considered only in patients with atrial fibrillation, to cont response, and not in patients in sinus rhythm.

In approximately 30% of patients, overt heart failure is precipitated by the onset of atrial fibrillation and in such patients, adequ heart rate and maintenance of sinus rhythm are beneficial. Pharmacotherapy with b blockers and amiodarone may be effective patients, atrioventricular modal ablation and pacemaker therapy should be considered.

In patients with sinus rhythm and relative tachycardia, a reduction in heart rate may be associated with improved ventricular fill hemodynamics, and b blocker therapy may be useful in such patients.

LV hypertrophy and increased LV mass are major pathophysiologic determinants of primary diastolic heart failure. Therapeutic to decrease LV hypertrophy and mass have potential benefits in the management of this syndrome. ACE inhibitors and AT1 re decrease LV wall thickness and mass and improve diastolic function in patients with hypertension. In some patients with diastc ACE inhibitors may decrease rehospitalization rates. In experimental studies, ACE inhibitors and AT1 blockers have been sho myocardial relaxation. Angiotensin I receptor blocking agents can improve exercise performance in patients with diastolic dysf hypertensive response to exercise.[31] A decrease in systemic arterial pressure in hypertensive or normotensive patients is ass improvement in diastolic function. Thus, some reduction of arterial pressure with ACE inhibitors, AT1 blockers, b blockers, nitra channel blockers is desirable.

Calcium channel blocking agents also can decrease LV hypertrophy ad mass and improve diastolic function.[32] However, long benefits of such therapy need to be determined. Heart rate-regulating calcium channel blocking agents, such as verapamil or c improve symptoms and LV diastolic function in some patients with hypertrophic cardiomyopathy.[33]

Interstitial fibrosis and increased myocardial collagen content are pathophysiologic contributing factors in primary diastolic hea Therapies with potential to decrease myocardial fibrosis and collagen content may be useful in the management of this syndro experimental studies, angiotensin inhibitors and aldosterone antagonists have been shown to decrease myocardial fibrosis an content.[34] However, clinical studies are lacking to demonstrate such benefits of these drugs in patients with established diast

failure.

Myocardial ischemia resulting from atherosclerotic CAD is a major mechanism of diastolic heart failure. Therapies to relieve my ischemia, either by decreasing myocardial oxygen demand (b blockers, nitrates, and calcium channel blockers) or by increasin perfusion (revascularization), are likely to be beneficial. However, improved outcome of such therapy needs to be demonstrate appropriate clinical studies.

As the long-term prognosis of patients with overt and severe diastolic heart failure is poor, preventive therapy should be consic at high risk of developing diastolic heart failure. Adequate treatment of hypertension, diabetes, and obesity and modification of factors for CAD should be and can be employed in clinical practice to prevent primary diastolic heart failure.

Conclusion

Primary diastolic heart failure is more prevalent in the elderly and is associated with variable mortality and morbidity. Hyperten without CAD, is the most frequent pathophysiologic association. CAD and increasing age are adverse prognostic factors. Treat present, are largely symptomatic. There is a need for prospective, controlled studies to assess the usefulness of various therap intervenes that are employed empirically. Preventive treatment should also be considered.

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Tables

Table 1.

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Table 1. Mechanisms of Hemodynamic Consequences in Primary Diastolic Heart Failure

Decreased LV compliance→disproportionate increase in LVDP→passive increase in LAP→PVP (signs and symptoms of pulmonary venous congestion)→post capillary pulmonary hypertension→secondary RV failure (signs and symptoms of systemic venous hypertension)
Restriction of ventricular filling→decreased preload→decreased stroke volume and cardiac output (signs and symptoms of low cardiac output)

LV=left ventricular; DP=diastolic pressure; LAP=left atrial pressure; PVP=pulmonary venous pressure; RV=right ventricular

Table 2.

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Table II. Criteria for Congestive Heart Failure Used in the Framingham Study*

Major Criteria	Minor Criteria	Major or Minor Criteria
Paroxysmal nocturnal dyspnea or orthopnea	Ankle edema	Weight loss >4.5 kg in 5 days in response to treatment
Neck vein distention	Night cough	
Rales	Dyspnea on exertion	
Cardiomegaly	Hepatomegaly	
Acute pulmonary edema	Pleural effusion	
S_3 gallop	Vital capacity decreased one half from maximal capacity	
Increased venous pressure >6 cm of water	Tachycardia (rate of >120/min)	
Circulation time >25 sec		
Hepatojugular reflux		

*For a definite diagnosis of congestive heart failure in this study, two major or one major and two minor criteria had to be present concurrently. Reprinted with permission from *N Engl J Med*. 1971;285:1441-1445.*

Table 3.

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Table III. Suggested Approaches in the Diagnosis of Primary Diastolic Heart Failure

Evidence of Congestive Heart Failure

- Clinical evaluation
- Cardiopulmonary exercise test along with pulmonary function tests in selected patients
- Exercise hemodynamics in selected patients
- Determination of brain natriuretic peptides in selected patients

Evidence of Preserved Left Ventricular Systolic Function

- Echocardiography (preferable)
- Radionuclide ventriculography in selected patients
- Contrast ventriculography in selected patients when cardiac catheterization is performed for other clinical indications

Evidence of Diastolic Dysfunction (Not Mandatory)

- Echo-Doppler studies (preferable)
- Radionuclide ventriculography in selected patients
- Cardiac catheterization in selected patients

To Exclude Specific Pathophysiologic Conditions

Examples:

- Hypertrophic cardiomyopathy: echocardiography
- Constrictive pericarditis: cardiac catheterization, magnetic resonance angiography
- Amyloidosis: cardiac biopsy
- Restrictive cardiomyopathy: cardiac catheterization

Table 4.

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Table IV. Age-Related Changes in Myocardial Structure and Neuroendocrine, Vascular, and Cardiac Function

CHANGES IN MYOCARDIAL STRUCTURE
Myocardial cell size: increased
Collagen content: increased
Sarcoplasmic reticular calcium ATPase (SERCA) activity: decreased
CHANGES IN NEUROENDOCRINE FUNCTION
Decreased β-adrenergic receptor and β-androgenic inotropic response
Increased angiotensinogen
Increased angiotensin-converting enzyme and angiotensin receptors
CHANGES IN VASCULAR AND CARDIAC FUNCTION
Decreased arterial compliance
Accentuated reflected or tidal aortic waves
Increased left ventricular mass
Unchanged contractility and ejection fraction
Decreased early filling and increased late filling

Table 5.

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Table V. Diastolic Heart Failure in the Community: Underlying Cardiovascular Diseases, Olmsted County, MN (1996–1997)

Left ventricular ejection fraction >45%
Females, 79.6±13.6 years
Males, 75.9±8.7 years
Hypertension without coronary artery disease: 26%
Hypertension with coronary artery disease: 36%
Hypertension with valvular heart disease: 15%
Diabetes: 16%
Hypertrophic/restrictive cardiomyopathy: 3%

Adapted with permission from *Circulation*. 2000;102:II-760[21]

Table 6.

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Table VI. Heart Failure With Preserved Systolic Function in African Americans: The Role of Diabetes Mellitus and Obesity

	CAUCASIANS	AFRICAN AMERICANS
Age (years)	71.8±12.9	69.6±12.8
Body surface area (m^2)	1.87±0.29	1.97±0.26*
Body mass index (kg/m^2)	28.7±7.4	31.6±9.3*
Severe obesity (%)	36	57*
Diabetes (%)	24	37*
Coronary artery disease (%)	31	24
Hypertension (%)	57	66

*Statistically significant difference
Adapted from *Circulation*. 2000;102:II-761[22]

Table 7.

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Table VII. Therapeutic Objectives and Potential Therapies for Primary Diastolic Heart Failure

To Relieve Congestive Symptoms
Diuretics, nitrates, angiotensin-converting enzyme (ACE) inhibitors, angiotensin II subtype 1 receptor blocking agents (AT_1 blockers)
To Improve Myocardial Relaxation (Lusitropic Agents)
Drugs with positive inotropic effects Beta-adrenergic agonists Phosphodiesterase inhibitors ACE inhibitors, AT_1 blockers
To Decrease Heart Rate and Improve Diastolic Filling
Beta blockers Heart rate-regulating calcium channel blockers
To Control Ventricular Response and/or Maintain Sinus Rhythm in Atrial Fibrillation
Beta blockers Amiodarone Heart rate-regulating calcium channel blockers Atrioventricular nodal ablation and pacemaker therapy
To Decrease Left Ventricular Hypertrophy and Mass
ACE inhibitors, AT_1 blockers Beta blockers Calcium channel blockers Any drug effective for adequate control of hypertension
To Decrease Myocardial Fibrosis and Collagen Content
ACE inhibitors, AT_1 blockers Aldosterone antagonists
To Decrease Myocardial Ischemia
To decrease myocardial oxygen demand: beta blockers, nitrates, calcium channel blockers To improve myocardial perfusion: revascularization therapy
To Prevent Primary Diastolic Heart Failure
Adequate treatment of hypertension, diabetes, and obesity and modification of other risk factors for coronary artery disease

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